UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/675,444	09/30/2003	Matthias Giese	APB-2	7837

7590 03/08/2007

O. M. (SAM) ZAGHMOUT PH.D
BIO INTELLECTUAL PROPERTY SERV ICE (BIO IPS)
8509 KERNON CT.
LORTON, VA 22079

EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,444	GIESE, MATTHIAS	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12 and 14-23* is/are pending in the application.

4a) Of the above claim(s) *21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12 and 14-20* is/are rejected.

7)☒ Claim(s) *1 and 3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 13 December 2006. Claims 2 and 13 have been canceled. Claims 1, 3-12, 14-23 are pending. Claims 21-23 are withdrawn. Claims 1, 3-12, and 14-20 are examined.

Applicants do not mention claims 24 and 25. If they are cancelled, please indicate on the record.

Claim Objections

Claim 1 is objected for grammatical error in the "which amount up to 10% of the nucleotide acids of the nucleotide sequences set forth in SEQ ID NO: 2." Examiner suggests amending the claim to read "which amount up to 10% of the entire sequence set forth in SEQ ID NO: 2."

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 3 contains open limitation but depends from claim 1, which has closed limitation.

Claim Rejections - 35 U.S.C. §112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-20 under 35 U.S.C. §112, second paragraph, as being indefinite is **withdrawn** in view of the amendment.

Claim 3 recites the limitation "said vaccine composition further comprises" in the second line. There is insufficient antecedent basis for this limitation in the claim.

Claims 1, 3-12, and 14-20 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." M.P.E.P. §2163.

The instant claims are directed to a vaccine composition consisting of ORF2, ORF5, and ORF7 of EAV, wherein ORF2 is the nucleotide sequence as set forth in

SEQ ID NO:2 or a functional variant thereof, wherein said variant carries nucleic acid exchanges, deletions or insertions which amount up to 10% of the nucleotide sequence set forth in SEQ ID NO:2.

The limitation "a functional variant thereof" encompasses all nucleotide sequences with at least 90% identity, or with at least 616 (684*90%) nucleotides as compared to SEQ ID NO: 2. Since there are 3 alternate nucleotides that can be substituted into each of the remaining 68 positions, the number of possible combinations is calculated by

3^{68} x 684!/68!(684-68-1)!

There are approximately $1.4x10^{130}$ variant nucleotide sequences with at least 90% identity to SEQ ID NO: 2. Thus, the claims are drawn to an enormous genus of amino acid sequences. The only factor present is the nucleotide sequence of SEQ ID NO: 2. There are still at least about $1.4x10^{130}$ other full-length sequences with at least 90% identity that are not described in the specification, let alone the fragments with at least 90% identity. Although the M.P.E.P. does not define what constitutes a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618. Therefore, a single sequence does not constitute a representative number of species to adequately describe such a highly variable genus of nucleotide sequences.

One skilled in the art cannot envision the chemical structures of the enormous genus of SEQ ID NO: 2 variants that correlate with the characteristic of protection against EAF infections in horses and induces a cellular immune response. Accordingly, Applicants are not in possession of the entire genus of the variants of SEQ ID NO: 2 at the time of filing the application.

Claim Rejections - 35 U.S.C. §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1, 3-8, 10 and 15-19 under 35 U.S.C. §102(b) as being anticipated by Tobiasch *et al.* (2001) is **withdrawn** in view of the amendment.

The rejection of claims 1, 4-10, 12 and 14-19 under 35 U.S.C. §102(a) as being anticipated by Giese *et al.* (2001) is **maintained** because Applicant's claim for foreign priority is not proper.

Applicant alleges that the foreign priority document, EP 02002250.5, filed on 20 January 2002, precedes the publication date of Giese *et al.*, which is October 2002. However, the foreign application is filed more than 12 months before the instant

application and is filed by a different inventor, BOEHRINGER INGELHEIM VETMEDICA GMBH.

Claims 1, 3-12, and 14-20 are rejected under 35 U.S.C. §102(b) as being anticipated by EP 02002250.5.

The instant claims are drawn to a vaccine composition, which is protective against equine arteritis virus (EAV) infections in horses and induces a cellular immune response, consisting of open reading frame nucleic acids (ORF) 2, SEQ ID NO:5 or SEQ ID NO:9 (ORF 5), and SEQ ID NO:7 (ORF 7) of EAV, wherein ORF 2 is the nucleotide sequence as set forth in SEQ ID NO:2 or a functional variant thereof, wherein said variant carries nucleic acid exchanges, deletions or insertions which amount up to he nucleotide acids of the nucleotide sequences set forth in SEQ ID NO:2.

EP 02002250.5 teaches vaccine compositions comprising open reading frame (ORF) 2, ORF 5 and ORF 7 nucleic acid of EAV, nucleic acid of said ORF2, ORF 5 and ORF 7 and vectors comprising said ORFs. The invention further relates to the use of said ORFs and vectors in the manufacture of a medicament for the prevention and treatment of EAV infections. See page 1, line 1-9. The invention further relates to a vaccine composition according to the invention as disclosed supra, wherein said vaccine composition further comprises one or several ORFs selected from the group of ORF 1a, ORF 1b, ORF 3, ORF 4, ORF 6. Any combination of said ORFs or all of said ORFs may be part of said vaccine. See page 8, line 21-24. The nucleic acid is cDNA. See page 8, line 42-43. The vaccine composition comprises one or several nucleic acid

vectors each comprising one or more ORFs, wherein said vector(s) is/are expression vector(s) that comprise(s) a eukaryotic *cis*-acting transcription/translation sequence functionally linked to said ORF(s), wherein said expression vector is selected from the group of pCR3.1, pcDNA3.1/His A, pcDNA3.1/His B, pcDNA3.1/His C, and pDisplay (pD). The invention further comprises the nucleic acid encoding interleukin 2 (IL-2) or a vector or expression vector comprising said nucleic acid encoding IL-2, pharmaceutically acceptable carrier or excipient, one or several adjuvants selected from the group of Muramyl Dipeptide (MDP), Montanide 720, Poly Inosine:Cytosine (Poly I:C) or plasmid DNA comprising unmethylated cytosine, guanine dinucleotide sequence motifs (CpG). See page 9, line 1-28. ORF2 is SEQ ID NO: 2, ORF 5 is SEQ ID NO: 5 or SEQ ID NO: 9 and ORF 7 is SEQ ID NO: 7. One example of a targeted delivery system for the EAV ORF nucleic acid/vector(s) is a cationic liposome. See page 10, line 23-24 and 26-34; and page 11, line 30-33.

Claim 3 is rejected under 35 U.S.C. §102(b) as being anticipated by Chirnside *et al.* (US 5,773,235; '235 patent).

The instant invention is set forth above. The '235 patent teaches recombinant DNA having use in provision of vaccines for EAV mediated disease. Column 1, line 5-5-9. The '235 patent further teaches cDNA encompassing EAV ORFs 2 to 7 cloned into the bacterial expression vectors. Column 4, line 8-11.

The rejection of claims 1, 3-8, 10, 13, 15-20, 24 and 25 under 35 U.S.C. §102(b), or alternatively, under 35 U.S.C. §103(a) as being obvious over Tobiasch *et al.* (2001) is **withdrawn** in view of the amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1, 3-8, 10, 11 and 15-19 under 35 U.S.C. §103 (a) as being obvious over Tobiasch *et al.* (2001) in view of Krieg *et al.* (1998) is **maintained** and extended to claim 20.

The instant invention is set forth above.

Examiner's rejection in the Action mailed on 05 June 2006 is as follows:

Tobiasch *et al.* teach prevention of EAV in horses by DNA vaccination. The cDNA sequence of ORF3, ORF4, ORF5, and ORF7 (Table 1) were molecularly cloned into the corresponding sites of expression vectors pCR3.1, pDisplay, and/or pcDNA3.1/HisC. See Abstract and on page 189-190, Molecular Cloning of Viral cDNA and Preparation of Plasmid DNA. The vaccine composition comprises one or several vectors, each comprising the aforementioned individual EAV ORF. See page 193, DNA Vaccination of Mice with Vector Construct Expressing Viral ORFs 5 and 7. The vaccine composition further comprises PBS (p. 191, DNA Vaccination of Animals), which is a pharmaceutically acceptable carrier or excipient.

Tobiasch *et al.* do not disclose any adjuvant in the vaccine composition. Krieg *et al.* suggest unmethylated CpG dinucleotides as adjuvant for DNA vaccines. Specifically, Krieg *et al.* disclose that CpG motifs can be added deliberately to DNA or conventional protein vaccines to enhance the Th1 immune response. See Abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the DNA vaccine composition of Tobiasch *et al.* by

adding CpG dinuleotides as taught by Krieg *et al.* The skilled artisan would have been motivated to do so to exert an essential endogenous adjuvant activity for the EAV ORF vaccines and to increase the efficacy of the EAV vaccine compositions. There would have been a reasonable expectation of success, given that CpG DNA can directly activate both B cells and monocytic cells including macrophages and dentritic cells (See Figure 1), as taught by Krieg *et al.* Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Applicants argues that the cited references do not suggest a vaccine composition or nucleic acid vector *consisting of* nucleic acid(s) encoding ORF 2, ORF 5 and ORF 7. Examiner respectfully disagrees. Although Tobiasch *et al.* do not expressly disclose a vaccine vector *consisting of* nucleic acid(s) encoding ORF 2, ORF 5 and ORF 7, they explicitly disclose that ORF 2 is in the same reading frame with ORF 5 and ORF 7 (Figure 1) and that ORF 2a is conserved in all arteriviruses. It would have been obvious to one skilled in the art to add ORF 2 into the vaccine taught by Tobiasch *et al.* The skilled artisan would be motivated to add the ORF 2 to increase the immunogenicity because ORF 2 (N-glycosylated minor membrane protein) and ORF 5 (N-glycosylated major membrane protein) are both membrane proteins. There would be reasonable expectation of success given that ORF 2 is highly conserved region, which would elicit immune response against any strain of arteriviruses.

Claims 9 and 12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Tobiasch *et al.* in view of Cantlon *et al.* (2000).

The instant invention is limited to further comprising the nucleic acid encoding equine IL-2 or a vector or expression vector comprising the IL-2-encoding nucleic acid.

The disclosure of Tobiasch *et al.* is set forth above. Tobiasch *et al.* do not disclose IL-2 in the vaccine against EAV. Cantlon *et al.* disclose that in mice, co-administration of a plasmid that expressed interleukin-2 resulted in a significant, though modest, increase in antibody titers relative to use of the G gene vaccine alone. See abstract.

It would be obvious to one skilled in the art at the time of invention to add a nucleic acid encoding equine IL-2 or a vector containing IL-2-encoding nucleic acid to the vaccine composition of EAV ORF 2, ORF 5, and ORF 7. One would be motivated to do so because Cantlon *et al.* suggest that IL-2-plasmid co-administration result in an increase in immune response.

Claim 14 is rejected under 35 U.S.C. §103(a) as being unpatentable over Tobiasch *et al.* in view of Gregoriadis *et al.* (1997).

The instant invention is limited to encapsulating the nucleic acid or vector vaccine into cationic liposomes. Tobiasch *et al.* do not disclose this feature.

Gregoriadis *et al.* disclose that antigen-coding vector entrapped into cationic liposomes leads to greatly improved humoral and cell-mediated immunity. See abstract.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
28 February 2007

Louise Humphrey, Ph.D.
Assistant Examiner